**REMARKS:**

Claims 9-10 and 14 are currently pending. Claims 9-10 and 14 are rejected. Claims 9 and 14 are amended.

**Claim Rejections under 35 USC § 112 ¶1**

Claim 9-10 and 14 are rejected for allegedly being not enabling because the Examiner believes that the instant Specification would not enable one of ordinary skill in the art to make the instant invention.

The Applicants respectfully disagree.

According to the Examiner the present claims are not enabled because it is not routine in the art to screen for multiple substitutions or multiple modifications, and the results of said modifications are unforeseeable since, according to the Examiner, the application does not give information about regions of the protein that can be modified and regions that need to be conserved. In this regard, the Examiner cites Greener et al. claiming that this method is time consuming and expensive, and would lead only to a limited number of random mutants. The Examiner further states that Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the Claims. Said Claims allegedly broadly include dihydroorotase (DHO) with an enormous number of amino acid modifications. Still further, the Examiner states that the scope of the Claims must bear a reasonable correlation with the scope of enablement citing *In re Fisher*.

In reviewing the Examiner's comments on about the instant rejections, it appears that the instant rejections relate more to the patentability of nucleic acids sequences per se (as compound Claims) rather than the method Claims of the instant invention. In the method of the instant invention, any plant DHO with a homology of at least 60% of SEQ ID NO: 1 can be used for the detection of inhibitors with no regard for the methods or protocols used to obtain said DHO. As disclosed in the instant Specification, the instant recited method allows a large number of chemical compounds to be tested for herbicidal properties; DHO is surprisingly a suitable target for new herbicides.



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The Examiner bases the instant rejection arguments on the fact that one of the components of the test system, DHO variants, which has a homology of at least 60% to SEQ ID NO: 1, is not available to one of ordinary skill in art. Applicants urge that the Examiner has merely stated the aforementioned reason for rejection but has failed to provide substantial reasons stating why the instant method is not enabled. Nonetheless, as Applicant explained in the reply to the previous Office Action, one of ordinary skill in the art can easily obtain probes from the sequences disclosed in the present application (e.g. SEQ ID NO: 1 from *S. tuberosum*, in the sequence listing; DHO from *A. thaliana*, page 2, line 9 of the instant Specification). It is routine for one of ordinary skill in the art to use such artificial generated probes to find DHO in plants other than *S. tuberosum* or *A. thaliana*. Furthermore, one of ordinary skill in the art can use the full length sequence (or parts of it) to find functional equivalent sequences in electronic publicly available databases. Accordingly, the skilled artisan can easily find functionally equivalent sequences from other plant species, which will be most likely not be identical with SEQ ID NO: 1 and thus, in contrast to the Examiner's assertions, said variants are readily available.

Applicants respectfully request clarification regarding Examiner's position for the rejections on this issue. Applicants wish to know whether the Examiner disagrees with the instant arguments or whether the Examiner wishes to obtain further information about these facts (e.g. information about how to search the databases, how to screen plant species other than *A. thaliana* or *S. tuberosum*).

In addition to the methods set forth above, one of ordinary skill in the art can easily obtain mutations based on already known sequences such as SEQ ID NO: 1. Applicants urge, again, that screening for mutant enzymes is routine for the skilled artisan and can be done, e.g. by *in vivo* mutagenesis, which is based on the use of *E. coli* strains having mutations in the genes for the DNA repair system (e.g. mutHLS, mutD, and mutt, *see* e.g. Rupp, W.D. (1996)). The use of this technique is illustrated in Greener et al. (1994).

The Examiner states that the aforementioned procedures are time consuming and expensive and would only lead to a limited number of mutations.

Applicants respectfully disagree.

As stated in Greener et al., the **formerly used PCR techniques** for generating random mutation



PAGE 8/10 * RCVD AT 12/21/2005 4:46:49 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-6/39 * DNIS:2738300 * CSID:2026590105 * DURATION (mm-ss):02-58

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are time consuming and expensive and lead only to a limited number of random mutants. In contrast the mutator strains such as XL1-Red have a high mutation rate (*see* page 7, left column, 2nd paragraph as follows) and are extremely easy and cost effective to handle (*see* page 33, left column, 3rd paragraph). Plasmids of XL1-Red can be isolated easily (e.g. by commercially available isolation kits in a very short period of lime) and transferred into *E. coli* strains for recombinant expression (e.g. in multiple well plates to enable a large number of clones to be analyzed). Simple tests for functionality (*see* e.g. those disclosed in the instant application on page 20-21, example 11) in high though put methods easily lead to a large number of functionally equivalent mutants of DHO. Said mutants can be used for the method of the present invention. Thus, the skilled artisan can easily obtain DHO sequences, which are not identical with SEQ ID NO: 1 or with the *A. thaliana* sequence for use in the method of the present invention.

More importantly though, the availability of DHO variants play only a minor role in the method of the instant invention. The instant invention recites a method and does not recite Claims for nucleic acid sequences.

In addition, in regards to the case law cited by the Examiner, *In re Fisher* does not disclose any substantial statements about enablement/utility that can be transferred to the present case. In contrast, according to the aforementioned decision, it is necessary to disclose a specific utility for a nucleic acid sequence, meaning one has to give a function of the sequence other than a general statement such as "can be used as a marker" to acquire compound protection for nucleic acid sequences.

Thus, since the instant invention does not recite compound Claims for nucleic acids and Applicants have provided a specific utility for the nucleic acid sequences Claimed in the process of the instant invention, thus, *In re Fisher* is not on point with the facts of the instant application and as such, should not be used as a determinative reference.

For at least the reasons stated above, it is urged that the rejections under 35 USC § 112 ¶1 should be withdrawn. Favorable action is solicited.



PAGE 9/10 * RCVD AT 12/21/2005 4:46:49 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-6/39 * DNIS:2738300 * CSID:2026590105 * DURATION (mm-ss):02-58

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**Claim Rejections under 35 USC § 112 ¶2**

Claims 9-10 and 14 are rejected for allegedly failing to point out and disitnently claim the subject matter which the Applicants regard as their invention.

Applicants respectfully disagree.

Nonetheless, the Examiner is directed to amended Claims 9 and 14 wherein the term "biological " has been amended to read "enzymatic" as per the Examiner's instruction in the instant Office Action. Also, the term "'absence' of a test" has been added tio Claim 9 as per the Examiner's instructions.

For at least the reasons stated above, it is urged that the rejections under 35 USC § 112 ¶2 should be withdrawn. Favorable action is solicited.



PAGE 10/10 * RCVD AT 12/21/2005 4:46:49 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-6/39 * DNIS:2738300 * CSID:2026590105 * DURATION (mm-ss):02-58

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